

REMARKS

This amendment adds, changes and/or deletes claims in this application. A detailed listing of all claims that are, or were, in the application, irrespective of whether the claim(s) remain under examination in the application, is presented, with an appropriate defined status identifier.

Amendments are proposed for claims 4 and 12. Claims 11-13 are withdrawn. Thus, after amending the claims as set forth above, claims 1-10 are now pending in this application.

Applicant respectfully requests reconsideration of the present application in view of the foregoing amendments and in view of the reasons that follow.

I. NEW RESTRICTION REQUIREMENT

The examiner asserts that prior amendment of claim 8 necessitated a new ground of rejection allegedly because the amendment changed the scope of the claim. The amendments merely changed the style of the claim, however, not its scope. Accordingly, applicants traverse the withdrawal of claim 8 and request reconsideration.

II. REJECTIONS UNDER 35 U.S.C. § 112 ¶1

The examiner rejects claim 4 for allegedly failing to convey to the skilled person that the applicants possessed the claimed invention at the time the application was filed. In particular, the examiner asserts that “the specification is silent as to the mutations that need to be detected for position 87 to be indicative of quinolone resistance.” As such information is well-known by those in the field, one of skill in the art would readily recognize that, as of the filing date, applicants possessed the claimed invention. Nevertheless, to advance prosecution in this case, applicants have amended claim 4 and believe the amendments obviate the rejection.

III. REJECTIONS UNDER 35 U.S.C. § 103

The examiner rejects claims 1-3, 5, 6, 8-10 under 35 U.S.C. § 103(a) for allegedly being unpatentable over Weigel et al. (WO 99/50458) in view of Chee et al. (A) (WO 95/11995) and Alberts et al. (Molecular Biology of the Cell). Applicants respectfully traverse the rejection.

The present invention is directed to a micro-array based method for detecting the presence of quinolone resistant *E. coli* strains in a biological sample. The present invention is based on the finding that all of the quinolone resistant *E. coli* strains exhibited mutations in the *gyrA* polypeptide in at least one of amino acids positions 83 and 87 (cf. [0017] of US 2005/0069897), which issue permits the generation of a limited number of capture probes (two sets of 64 polynucleotides) to be attached on a micro-array.

WO 99150458 (Weigel et al.) pertains to oligonucleotide probes suitable for detecting Enterobacteriaceae and quinolone-resistant Enterobacteriaceae. Figures 2 and 3 describe some particular nucleic acid mutations in different Enterobacteriaceae resulting in different amino acids at positions 83 and 87 of *gyrA*. In addition, the figures refer to a broad variety in other positions, such as positions 85 and 89 of *gyrA*, without suggesting any relationship between mutations in these and those of positions 83 and 87. The only quinolone resistance conferring mutations with respect to different *E. coli* strains are mentioned in Fig. 4a (Ser⁸³ to Leu and A⁸⁷ to Gly, Tyr and Asn).

According to the teaching of Weigel et al., the other mutations shown Fig. 2 and 3 are suitable to distinguish between a number of different Enterobacteriaceae, namely *E. coli*, *C. freundii*, *E. aerogenes*, *E. cloacae*, *K. oxytoca*, *K. pneumoniae*, *P. stuartii* and *S. marescens*, in that said Enterobacteriaceae are distinguishable by a specific nucleotide sequence at amino acid positions 83 and 87 of *gyrA*, which issue renders said positions clearly not suitable to reveal quinolone resistant *E. coli* strains only.

Based on the teachings of Weigel et al. alone the skilled person would expect that other mutations in said amino acid positions would rather be suitable in identifying other Enterobacteriaceae than such mutations would (1) occur in *E. coli* only and (2) merely characterize resistance determinants than a possibility to distinguish different *E. coli* strains from each other. In addition, there is no indication in said document that all mutations, *i.e.* 64 for each of the two amino acid positions, might occur.

WO 95/11995 (Chee et al. (A)) is directed to arrays of nucleic acid probes on biological chips. The nucleic acid probes comprise permutations of each nucleotide position in order to permit DNA sequencing. Chee et al. (A) as well as Alberts et al. (Molecular Biology of the Cell, (1994) third edition, Garland Publishing, p. 106), Routier et al. (Nucleic Acids Research, 27 (1999), pp. 4160-6) and Chee et al. (B) (Science et al., 274 (1996), pp. 61.0-4) are silent about detecting any kind of antibiotic resistance such as quinolone resistance. Thus, nothing in the cited material would have encouraged the skilled person to combine those teachings with that of Weigel et al.

Accordingly, applicants request that the rejection be withdrawn.

Applicants believe that the present application is now in condition for allowance. Favorable reconsideration of the application as amended is respectfully requested.

The examiner is invited to contact the undersigned by telephone if it is felt that a telephone interview would advance the prosecution of the present application.

The Commissioner is hereby authorized to charge any additional fees which may be required regarding this application under 37 C.F.R. §§ 1.16-1.17, or credit any overpayment, to Deposit Account No. 19-0741. Should no proper payment be enclosed herewith, as by a check or credit card payment form being in the wrong amount, unsigned, post-dated, otherwise improper or informal or even entirely missing, the Commissioner is authorized to charge the unpaid amount to Deposit Account No. 19-0741. If any extensions of time are needed for timely acceptance of papers submitted herewith, applicants hereby petition for

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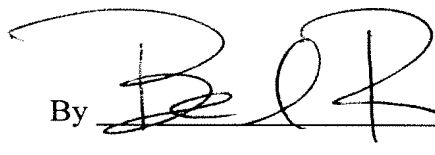
such extension under 37 C.F.R. § 1.136 and authorize payment of any such extensions fees to
Deposit Account No. 19-0741.

Respectfully submitted,

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